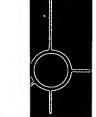
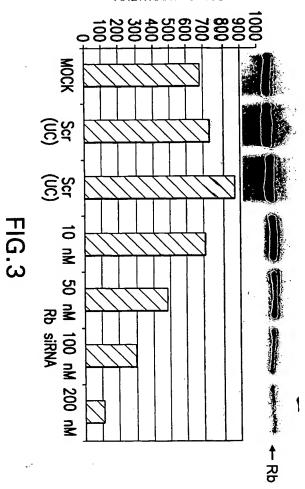


FIG.2









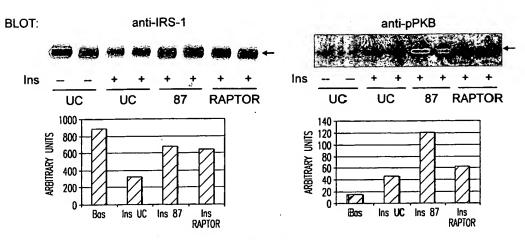


FIG.4

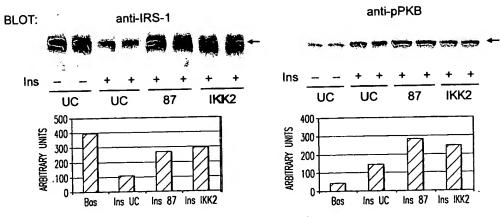
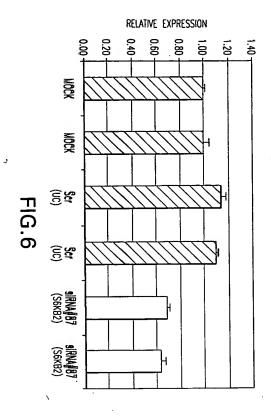


FIG.5





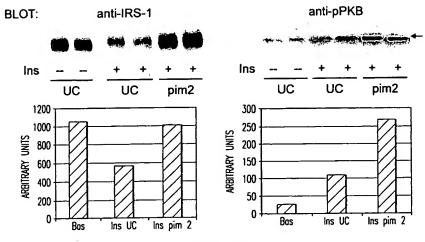


FIG.7

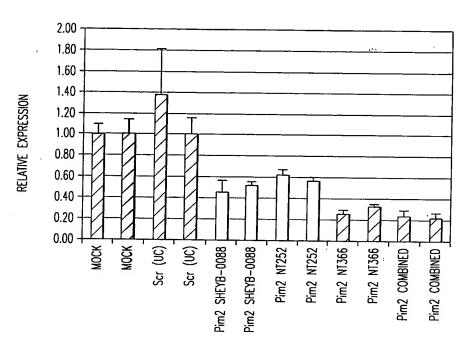
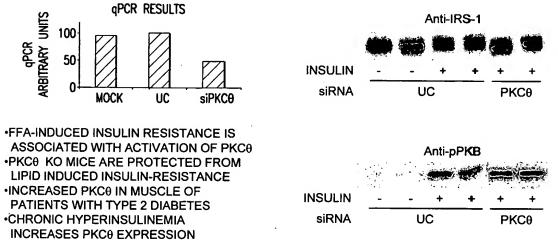


FIG.8

## REDUCTION OF PKC0 INHIBITS IRS-1 DEGRADATION AND ENHANCES INSULIN-INDUCED PKB PHOSPHORYLATION



**FIG.10** 

# **5**

### REDUCTION OF IKK2 INHIBITS IRS-1 DEGRADATION AND ENHANCES INSULIN-INDUCED PKB PHOSPHORYLATION

- OVEREXPRESSION OF IKK2 CAUSE INSULIN RESISTANCE
- EXPRESSION OF DOMINANT NEGATIVE IKK2 REVERSES TNF, FFA AND HYPERGLYCEMIA INDUCED RESISTANCE
- IKK2 HAS BEEN SHOWN TO BE A TARGET OF HIGH DOSE SALICYLATES
- HETEROZYGOUS DELETION (ikkbeta+/-)
  PROTECTED AGAINST THE
  DEVELOPMENT OF INSULIN RESISTANCE
  DURING HIGH-FAT FEEDING AND IN
  OBESE (ob/ob) MICE

Anti-pPKB

- + +

siRNA UC IKK2

FIG.11

SALT-INDUCIBLE KINASE-1 (SIK) IS A NEW KINASE INVOLVED IN INSULIN RESISTANCE

Anti-pPKB	+ + +	A UC SIK	enal glands	hat belongs		se tissues,	etic animals	of Ser789	als
Anti-IRS-1	INSULIN - + + + + - INSULIN	SIRNA UC SIK SIRNA	•SIK was first cloned from the adrenal glands	•Serine/threonine protein kinase that belongs	to AMPK family	<ul> <li>SIK1 mRNA is elevated in adipose tissues,</li> </ul>	livers, and skeletal muscle of diabetic animals	<ul> <li>Involved in the phosphorylation of Ser789</li> </ul>	in IRS-1 in livers of diabetic animals

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